



THE OCULAR IMMUNOLOGY
AND UVEITIS FOUNDATION
Dedicated to Eye Disease Cure and Education

Growth Factors, Corneal Wound Healing, and Persistent Epithelial Defect

Arash Maleki, MD; C. Stephen Foster, MD, FACS, FACR

April 2026

The corneal epithelium is constantly renewed by limbal stem cells, which move toward the center and divide to replace surface cells. Under normal conditions, this regenerative process allows epithelial defects to heal quickly, usually within seven to ten days. When this healing process is impaired, recovery is delayed and can lead to a persistent epithelial defect (PED), typically defined as a defect that does not resolve after two weeks despite appropriate treatment. This condition may occur in a variety of clinical situations, and treatment of the resultant persistent epithelial defects can be extraordinarily frustrating to even the most knowledgeable cornea and external disease expert.

PEDs are clinically important because they can lead to ongoing discomfort, photophobia, and decreased visual acuity, while also increasing the risk of microbial keratitis and corneal perforation. Their development is multifactorial, stemming from either insufficient epithelial cell production by limbal stem cells or an ocular surface environment that fails to support epithelial survival. Systemic conditions (diabetes, autoimmune diseases, chemotherapy, and immunosuppressive therapy), ocular conditions (limbal stem cell deficiency, congenital aniridia, neurotrophic keratopathy, infectious keratitis, exposure keratopathy, and cicatrizing disorders (ocular pemphigoid or trachoma) are risk factors for PED.

In regard to management, discontinuation of potentially toxic medications, treatment of surface desiccation and exposure, protection of the ocular surface through bandage soft contact lenses, and tarsorrhaphy, and suppression of chronic inflammation usually will result in closure of epithelial defects, but a significant number of patients exist in whom these measures are insufficient to achieve that desired goal.

For this reason, interest in “growth factors” which might enhance epithelial mitosis, epithelial migration, and epithelial adhesion to the underlying substrate has been of substantial interest for the past 2 decades. Despite this interest, we still lack some magic elixir, the application of which will consistently promote closure of a persistent epithelial defect. Fibronectin therapy, for example, was a disappointment in randomized, masked, placebo-controlled trials, as was epidermal growth factor.

Amniotic membrane transplantation and limbal stem cell grafting, using a range of techniques, have been widely employed with strong success in treating PEDs arising from various underlying ocular or systemic conditions.

A nerve growth factor, Oxervate (cenegermin), was approved by the FDA in 2018, for the treatment of PED and neurotrophic keratitis, becoming the first-in-class topical biologic for this condition.

Evidence indicates that growth factors, particularly Insulin-like Growth Factor (IGF) and Fibroblast Growth Factor (FGF), alongside fetal umbilical cord blood serum (UCBS), are increasingly utilized in ophthalmology for ocular surface repair and tissue regeneration. These agents are recognized for their roles in promoting cell proliferation, migration, and differentiation to treat severe ocular surface diseases (OSD) and PEDs.

In truth, problems with the ocular surface are commonly complex. We believe that a case-by-case analysis of each individual with PED will be essential in order for the clinician to develop a clear sense of the factors contributing to the failure for the wound to close, with subsequent attention to each of the factors contributing to that failure.

We currently have three prospective trials ongoing in the care of patients with non-healing corneal epithelial defects.

References:

- 1) Yoon KC. Use of umbilical cord serum in ophthalmology. *Chonnam Med J.* 2014;50(3):82-5.
- 2) Moin KA, Pandiri S, Manion GN, Brown AH, Moshirfar M, Hoopes PC. The Utilization of Topical Insulin for Ocular Surface Diseases: A Narrative Review. *Cureus.* 2024;16(6):e62065.
- 3) Vaidyanathan U, Hopping GC, Liu HY, Somani AN, Ronquillo YC, Hoopes PC, Moshirfar M. Persistent Corneal Epithelial Defects: A Review Article. *Med Hypothesis Discov Innov Ophthalmol.* 2019;8(3):163-176.
- 4) Vaidyanathan U, Hopping GC, Liu HY, Somani AN, Ronquillo YC, Hoopes PC, Moshirfar M. Persistent Corneal Epithelial Defects: A Review Article. *Med Hypothesis Discov Innov Ophthalmol.* 2019 Fall;8(3):163-176.
- 5) Gurnani B, Feroze KB, Patel BC. Neurotrophic Keratitis. 2025 Mar 27. In: *StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026.*